REMARKS

Claims 55, 56, 58, 60-66 and 68-73 are pending in the instant application. Claims 55, 56, 58, 60-66 and 68-73 have been rejected. Claims 55, 63, 65, 68 and 73 have been amended. Claims 56, 64 and 69 have been cancelled without prejudice. Claims 74-75 have been added. Support for these amendments is provided throughout the specification and in particular at pages 5-8 and the Example beginning at page 10. Thus, no new matter is added by these amendments and entry is respectfully requested. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Objection to Claims 56 and 69

Claims 56 and 69 have been objected to as reciting the linking of three items, the heavy and light chains and a secretion signal, through a single linker. It is respectfully pointed out that these claims have been cancelled, thus mooting this objection.

Withdrawal is therefore respectfully requested.

II. Rejection of Claims under 35 U.S.C. 112, second paragraph

Claims 55, 56, 58, 60-66 and 68-73 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, claim 55 has been rejected for the phrase "administering to an animal", while the antibody is expressed in fish. Thus, in an earnest effort to advance the prosecution of this case, and in accordance with the Examiner's suggestion, Applicants have amended the claim to state --administering to a fish--.

Claims 55 and 68 have also been rejected for recitation of "a recombinant antibody molecule derived from an antibody . . . " as it is unclear what is encompassed by derived. According, claims have been amended to clarify that the recombinant antibody molecule is derived from the variable domains of immunoglobulin heavy and light chains of an antibody raised against the disease-causing virus.

Claims 63 and 73 have been rejected for recitation of a monoclonal antibody derived from 3F1H10 "with two amino acid substitutions . . " as the Examiner suggests that it is unclear whether the derived monoclonal antibody or the 3F1H10 molecule contains the substitutions. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended these claims to clarify that the sequence encoding the variable domain of the heavy chain contains these substitutions.

Claims 63 and 73 have been rejected for recitation of the phrase "and comprises a secretion signal of rainbow

trout . . ." as the Examiner suggests that it is unclear whether the plasmid comprises such signal or the antibody. Accordingly, in an earnest effort to advance the prosecution, Applicants have amended claim 63 to state -- further encodes a secretion signal of rainbow trout transforming growth factor (TGF-beta) operably linked to the 5' end of the heavy chain gene--. Claim 73 has also been amended and this phrase had been deleted.

Finally claim 68 has been rejected for lack of antecedent basis for the term "fish". Claim 68 has been amended and this term has been deleted.

Withdrawal of these rejections under 35 U.S.C. 112, second paragraph is therefore respectfully requested.

III. Rejection of Claims 55-56, 58, 60-66 and 68-73 under 35 U.S.C. 112, first paragraph - Lack of Enablement

The rejection of claims 55-56, 58, 60-66 and 68-73 under 35 U.S.C. 112, first paragraph, has been maintained. The Examiner has acknowledged the specification to be enabling for a composition for protection of fish against viral haemorrhagic septicaemia virus comprising a non-infectious DNA nucleic acid construct encoding the single chain antibody 3F1H10 that recognizes VHSV, the DNA sequence for the antibody listed on pages 9-10 of the specification

and which comprises substitutions of asparagine 35 with threonine and lysine 64 with threonine and is linked at the 5'end to the secretion signal of transforming growth factor beta, and which sequence is operably linked to the CMV Promoter and a poly A tail for protecting a fish against VHSV infection. The Examiner has acknowledged the specification to be enabling for vaccines comprising these compositions and methods of providing prophylactic treatment of fish against VHSV by the administration of these compositions, by injection into the epaxial muscles below the dorsal fin, which compositions transform cells of the muscle tissue local to the injection site and produce secreted 3F1H10 antibodies, thereby producing protection against VHSV, as well as the plasmid vector construct itself. However, the Examiner suggests that the specification does not reasonably provide enablement for a plasmid encoding any antibody, any secretion signal sequence, any promoter sequence, any form of administration, any form of composition, treatment of any animal or any form of treatment for any disease-causing agents.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the claims to more precisely define the invention in accordance with the working example provided in the instant specification.

In particular, independent method claim 55 has been amended to state that the antibody is secreted, that it is a single chain antibody and that it comprises variable domains of immunoglobulin heavy and light chain polypeptides linked together by a linker peptide sequence as well as a secretion signal peptide at the N-end of the antibody molecule. Further, claim 55 had been amended to clarify that the recombinant antibody molecule is expressed in and secreted from transfected cells of the fish in vivo and that the construct is administered in the form of purified plasmid DNA to the fish.

In addition, the independent plasmid construct claim, claim 68 has been amended to state a non-infectious eukaryotic expression plasmid construct comprising a DNA sequence encoding a recombinant viral haemorrhagic septicaemia virus VHSV-neutralising single chain antibody molecule comprising variable domains of immunoglobulin heavy and light chains derived from the variable domains of the immunoglobulin heavy and light chain of monoclonal antibody 3P1H10 which are operably linked together by a linker and with the secretion signal of rainbow trout transforming growth factor (TGF-beta) operably linked to the N-terminal of the heavy chain.

The claims, as amended, more precisely define the antibodies and set forth the requirements for a secretion signal as well as its linkage to the construct, thus addressing the Examiner's concerns regarding breadth of the claims. Further, the claims make clear that the construct administered is a plasmid DNA, which is by definition double stranded, thus mooting any concerns regarding successful integration of gene therapies as set forth at page 9 of the Office Action. The claims as amended also clarify that the antibodies are secreted, thus addressing concerns raised at pages 10-11 of the Office Action regarding efficacy and intrabodies. In addition, the claims as amended relate to the working examples in the specification demonstrating efficacy, thus overcoming concerns regarding a lack of other working examples in the prior art. Finally, the claims as amended are limited to fish and viral disease in fish, thus addressing the Examiner's concerns regarding treatment of any animal and any disease.

Accordingly, the claims as amended herein meet the enablement requirements of 35 U.S.C. 112, first paragraph.

Withdrawal of this rejection is therefore respectfully requested.

IV. Rejection of Claims 1, 15, 21 and 24 under 35 U.S.C. 102(b)

Claims 1, 15, 21 and 34 are suggested to remain rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,543,144. It is respectfully pointed out, however, that these claims are not pending in the instant application. Accordingly, clarification as to what claims, if any, this rejection pertains to is respectfully requested.

It is respectfully pointed out that the pending plasmid construct claims, claims 68-75, specify a construct neither taught nor suggested by U.S. Patent 5,543,144. Thus, Applicants believe that the claims as presented herein are not anticipated by U.S. Patent 5,543,144 and withdrawal of this rejection is respectfully requested.

VI. Rejection of Claims 55-56, 58, 60-62, 64-66 and 68-72 under 35 U.S.C. 103(a)

Claims 55-56, 58, 60-62, 64-66 and 68-72 have been rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/37234.

Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obvious, three basic criteria must be met. First there must be some suggestion

or motivation to modify the teachings of the reference. Second, there must be a reasonable expectation of success. Finally the prior art must teach or suggest all the claim limitations. MPEP §2143.

As discussed in Section III, pending claim 55 has been amended to state a method for passive immunisation of a fish against a disease-causing virus in fish which comprises administering to the fish a non-infectious eukaryotic expression plasmid construct comprising a DNA sequence encoding a secreted recombinant single chain antibody molecule, wherein the antibody molecule comprises variable domains of immunoglobulin heavy and light chain polypeptides linked together by a linker peptide sequence and a secretion signal peptide at the N-end of the antibody molecule. Further claim 55 specifies that the recombinant antibody molecule is expressed in and secreted from transfected cells of the fish in vivo upon administration of said construct in the form of purified plasmid DNA to the fish.

Claim 68 has been amended to state a non-infectious eukaryotic expression plasmid construct comprising a DNA sequence encoding a recombinant viral haemorrhagic septicaemia virus VHSV-neutralising single chain antibody molecule comprising variable domains of immunoglobulin heavy and light chains derived from the variable domains of the

immunoglobulin heavy and light chain of monoclonal antibody 3F1H10 which are operably linked together by a linker and with the secretion signal of rainbow trout transforming growth factor (TGF-beta) operably linked to the N-terminal of the heavy chain.

In contrast teachings of Duan are related to intracellular immunization, and in particular to immunization against human immunodeficiency virus. There is no teaching or suggestion in the reference of immunization of fish. Nor is there any teaching in this reference of immunization against viruses in fish. Further, all teachings relating to secretion signals in this reference are general teachings with no detail regarding point of linkage and Duan teaches away from their inclusion in their constructs for intracellular immunization.

Thus, this reference does not teach or suggest all the limitations of the invention as now claimed. Further, this reference provides no reasonable expectation of success with respect to the invention as now claimed or motivation to modify the reference teachings to arrive at the instant claimed invention.

Accordingly, this reference cannot establish a prima facie case with respect to the instant claimed invention. See MPEP 2143.

Withdrawal of this rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

VII. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Advisory Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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